FORM PTO-1390U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE
(REV 5-93)

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER
9052-89

U S APPLICATION NO. (If known, see 37 C.F.R. 1.5)
09/914330

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/GB00/00577	February 18, 2000	February 25, 1999

TITLE OF INVENTION
ANALYTICAL INSTRUMENT

APPLICANT(S) FOR DO/EO/US
Philip Stephen GOODALL and Barry Leonard SHARP

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.

2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.

3. [X] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).

6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. [X] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [X] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.

8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98.

12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. [X] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.

14. [ ] A substitute specification.

15. [ ] A change of power of attorney and/or address letter.

16. [ ] Other items or information:

U.S. APPLICATION NO (If known, see 37 C F R 1 50)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/914330	PCT/GB00/00577	9052-89

	CALCULATIONS	PTO USE ONLY
17. [X] The following fees are submitted:		
Basic National Fee (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO **$860.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) **$690.00**		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) **$710.00**		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$100.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	**$860.00**	
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	**35** -20 =	**15**	**X $18.00**	**$270.00**	
Independent Claims	**3** -3 =	**0**	**X $80.00**	$	
Multiple dependent claim(s) (if applicable)			**+ $270.00**	$	
TOTAL OF ABOVE CALCULATIONS =				$	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$	
SUBTOTAL =				$	
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$	
TOTAL NATIONAL FEE =				$	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$	
TOTAL FEES ENCLOSED =				**$1,130.00**	
				Amount to be refunded	$
				charged	$

a. [X] A check in the amount of **$1,130.00** to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-0220.

NOTE: **Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.**

SEND ALL CORRESPONDENCE TO:

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"Express Mail" mailing label number EL733099418US
Date of Deposit August 24, 2001

I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C F R 1 10 on the date indicated above and is addressed to Commissioner for Patents, Washington, D C 20231

Date 8/24/01

SIGNATURE

Julie H. Richardson

Julie H. Richardson

40,142
REGISTRATION NUMBER

PTO FORM-1390 (REV 5-93)

Attorney's Docket No. 9052-89 PATENT

IN THE UNITED STATES DESIGNATED OFFICE (DO/US)

In re: Application of Goodall et al.
Serial No.: To be Assigned
Filed: Concurrently Herewith
For: ANALYTICAL INSTRUMENT

Date: August 24, 2001

BOX PCT
Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Sir:

Prior to the examination of the above application and calculation of claim fees, please amend the above-identified application as follows:

In the Specification:

At page 1, line 3, after the title and before the first sentence, please insert:

--Related Applications

This application claims priority from PCT Application Serial No. PCT/GB00/00577 filed 18 February 2000; the application was published in English under PCT Article 21(2). The international application claims priority from GB Application Serial No. 9904289.7 filed 25 February 1999. The contents of these applications are hereby incorporated by reference as if recited in full herein.

Field of the Invention--

At page 1, line 6, please insert,

--Background of the Invention--.

At page 2, line 1, please insert,

-- Brief Description of the Figures

Figure 1 is a schematic of a coincidence laser spectrometer according to embodiments of the present invention.

Figure 2 is a schematic of a multi-detector head according to embodiments of the present invention.

Detailed Description of Embodiments of the Invention--.

In the Claims:

Please cancel Claim 35.

REMARKS

Claims 1-34 are presented for examination. The specification has been amended above to add section titles to conform to U.S. practice. Applicant respectfully submits that the application is in condition for, and respectfully requests, substantive examination on the merits.

Respectfully submitted,

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CERTIFICATE OF EXPRESS MAILING

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I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box PCT, Commissioner for Patents, Washington, DC 20231.

Joyce Paoli

ANALYTICAL INSTRUMENT

This invention relates to a novel analytical instrument, and to novel methods of measuring, *inter alia*, low concentrations of stable and radioisotopes and/or low abundance isotopes.

The determination of radionuclides at environmental levels using classical radiometric counting is well established and likely to remain the method of choice for short half-life species. However, innovations in analytical instrumentation in the last ten years have the potential to replace radiometric counting for a wide range of longer half-life species.

Elemental and isotopic analysis has advanced significantly with the introduction of plasma source mass spectrometry. A variety of plasmas have been used as ionization sources, e.g., glow discharges, microwave induced plasmas, but the inductively coupled plasma (ICP) is the most widely accepted, and *de facto*, the preferred ion source for atomic mass spectrometry. The inductively coupled plasma is compatible with solid, liquid or gaseous sample introduction and is a robust and efficient ionization source for atomic mass spectrometry.

For some potential applications of plasma mass source spectrometry, *e.g.*, environmental and biomedical monitoring of radioisotopes, current techniques may not possess the required detection limits or selectivity. Classical radiometric techniques may provide the required detection limits, but do so at the expense of protracted count times and extensive sample preparation and clean-up. For example, within a plutonium bioassay program, current radiometric methods offer detection limits of 500 μBq per litre, but require 1-2 days of sample preparation and radiometric count times of, *e.g.*, four days with α-spectrometry and up to 28 days for α-track counting. There is a requirement to develop plasma source mass spectrometry to provide enhanced selectivity and improved detection limits without sacrificing the inherent flexibility, rapidity and robustness of the technique.

The instrument of the invention is designed to measure isotopes at extremely low concentrations and isotopes of very low abundance. An example of this would be the ultra low level determination of the radionuclides. The increasing interest in the behaviour of radionuclides in the biosphere requires that new methods be developed that have detection limits equivalent to, or better than, that of the existing techniques, but combine this with superior speed and a reduced cost of analysis. Improvements in speed are essential to enable wider screening, plant and event management and to monitor illicit uses of nuclear materials. The recent OSPAR agreement has committed the UK to real reductions in levels of liquid effluent discharges. For many radionuclides, conventional radiochemical analysis will limit the ability to demonstrate that such reductions have been achieved.

To achieve the aim of improved detection limits in plasma source mass spectrometry, the factors that limit the selectivity and sensitivity of inductively coupled plasma mass spectrometry (ICP-MS) were considered. The instrumental detection limits available from ICP-MS are, in most cases, limited by the background count and not the magnitude of the analytical signal derived from the ions of interest. The background is derived broadly from three distinct sources:

1. A non-specific instrumental background.

2. Interferences from atomic or molecular ions of the same nominal mass to charge ratio, consequent upon insufficient mass spectral resolution. Examples of these "isobaric" interferences include atomic ions such as; $^{241}Am^+$, $^{241}Pu^+$; $^{90}Sr^+$, $^{90}Zr^+$; $^{55}Fe^+$, $^{55}Mn^+$; ^{40}Ca, ^{40}Ar; $^{204}Pb^+$, $^{204}Hg^+$ or molecular ions such as $^{238}U^1H^+$, $^{239}Pu^+$; $^{40}Ar^{16}O^+$, $^{56}Fe^+$, $^{40}Ar^{35}Cl^+$, $^{75}As^+$

3. Isotopes of different nominal masses but present at high relative abundances, consequent upon insufficient abundance sensitivity. For example, ^{88}Sr; ^{89}Sr, ^{90}Sr; $^{55}Fe^{+}$, $^{56}Fe^{+}$.

These observations are the key to the development of instrumentation with the superior detection limits required for determination of radionuclides at background environmental and biomedical concentrations by ICP-MS techniques.

A comparison of alternative techniques to plasma source mass spectrometry suggests that resonance ionisation mass spectrometry (RIMS) offers similar or better absolute detection limits than achieved with current generation ICP-MS instruments, *e.g.* about 4×10^6 atoms for ^{239}Pu. The singular advantage of RIMS over, for example, ICP-MS, is the greater isotopic selectivity derived from the laser induced ionisation process. However, the prior chemical separation, though less demanding than that required by radio-chemical methods, is nevertheless time consuming and requires specific recovery of the element, deposition onto a Ta foil and overplating with Ti. Accelerator mass spectrometry (AMS) offers absolute detection power of the order of 10^6 atoms. Selectivity is achieved through the use of high energy dissociation of molecular ions and avoidance of isobars through negative ion discrimination. Improved detection limits are obtained by high energy counting to discriminate against detector background. High abundance sensitivity is achieved by acceleration to high potentials thus minimizing the relative ion energy spread. However, AMS involves large, complex and costly instrumentation. Sample preparation is complex and time consuming, requiring preparation of the element in a pure form. For these reasons, AMS is restricted to highly specialized roles and cannot at this time be considered as a laboratory scale or general purpose instrument.

Thus, we have now developed an analytical instrument and an analytical approach that overcomes or mitigates the problems with conventionally known instruments and techniques. As a technology demonstration, this new device is based upon an ICP-MS instrument, but is equally applicable to other forms of plasma mass

spectrometry. Indeed, the range of applications includes all forms of atomic mass spectrometry and molecular mass spectrometry. This instrumentation also provides a flexible platform for spectroscopic studies of atoms and molecules to determine fundamental parameters.

Thus according to the invention, we provide an instrument comprising an Inductively Coupled Plasma Source Mass Spectrometer equipped with a multi-dimensional detector system wherein ions transmitted by the mass spectrometer are detected with high selectivity.

The instrument is provided preferably with detectors which are based upon specific detection of transmitted ions, *e.g. via.* optical spectroscopy. The device is in principle, an ICP-MS instrument operating in a multi-dimensional detection mode and including the following:

- A conventional non-specific ion detection device.

- A device based upon optical spectroscopy to provide highly selective and specific detection of ions transmitted by the mass spectrometer.

The detector device based upon optical spectroscopy provides:

- A high resolution detection system, which in conjunction with conventional mass spectrometry, is capable of resolving ions of interest from interfering molecular ions of similar nominal mass to charge ratio.

- A high resolution spectroscopy system, which in conjunction with conventional mass spectrometry, is capable of resolving ions of interest from atomic ions of similar nominal mass to charge ratio.

- A high resolution spectroscopy system, which in conjunction with conventional mass spectrometry, provides very high abundance sensitivity.

Operation of the two detection systems as a single integrated coincidence detector that provides:

- Background count rates that are orders of magnitude lower than those obtained if the individual detection systems were used as isolated, individual detectors.

The descriptive term for this approach is Inductively Coupled Plasma Mass Spectrometry Coincidence Laser Spectroscopy (ICP-MS-CLS).

Thus, according to a preferred feature of the invention, we provide an ICP- MS-CLS instrument. We especially provide an ICP-MS-CLS instrument with a conventional non-specific ion detection device and a device based on optical spectroscopy as hereinbefore defined.

The instrument of the invention supplements the universal ion counting detector with one that has a high degree of species selectivity. The use of a detector based on resonance scattering from the ions to be detected, *e.g.*, laser induced fluorescence (LIF), provides vastly improved selectivity thereby removing the problem of isobaric interferences derived from either atomic or molecular ions. Additionally, by operating the optical detector in time correlation with a second detector, background count rates can be reduced by several orders of magnitude.

The instrumentation takes advantage of improved detector technology to achieve very high spatial and temporal resolution in the optical spectroscopy. This allows coincidence detection from single photons. This capability is important in that it allows the detection of ions in which there is a high probability of trapping in a

metastable state. Ions in metastable states are transparent to the exciting laser and thus the overall photon multiplicity from these ions is low.

To allow for efficient interaction between the laser and ion beam, the ion beam must be defined accurately in space and be focussed to approximately the beam diameter of the laser. An imaging spectrometer provides an ideal solution and a sector mass spectrometer is one such device. A commercial, double focussing, sector ICP-MS provides the basic platform for development of ICP-MS-CLS.

A key feature of this instrument is the manipulation of the ion energies. To couple efficiently the energy from the laser into the ion to be detected, the optical bandwidths have to be matched. For example, an ion beam of energy of 5000 ± 2.5 eV, has a Doppler spread of about 100 MHz for an ion of mass = 240. This is in excess of the natural line width which is off the order of 15 MHz. The ion energies were manipulated by two devices. The first involves the introduction of a collision/reaction cell to act as an ion bridge between the sampler/skimmer plasma interface and the mass spectrometer. This thermalises the ions and reduces their energy spread to less than 1 eV. Additionally, it enables selective gas phase chemistry to dissociate interfering molecular ions. The second method involves acceleration of the ions to compress the optical bandwidth of the ions to be detected. For example, an ion beam of mass 240 but with a 40 000 ± 5 eV energy range has a corresponding Doppler spread of about 37 MHz. In practice, by using a collision/reaction cell, lower standing voltages, *e.g.*, 10kV, can be employed. Assuming an ion energy spread of, *e.g.*, 1 eV, at 10 kV, the Doppler spread is about 15 MHz which approximates natural line widths.

Programmed acceleration of the ions within the optical detector is important and ensures that the ions to be detected come into resonance with the exciting laser within the detection volume of the optical detector. This prevents optical trapping of the ions prior to their arrival in the detection volume of the optical detector.

The abundance sensitivity of the spectrometer can be improved by three methods:

- Where the analyte exhibits an isotope shift, the ion of interest can be brought into resonance selectively.
- Selective excitation of one hyperfine branch of an ion of interest can also be used to increase the selectivity of the mass spectrometer.
- Many ions do not exhibit an isotope shift that can be resolved optically, but acceleration of the ions induces an isotope shift by Doppler shifting the resonant frequency of the low abundant ion away from the interfering major isotope.

Where optical trapping of the ions of interest becomes significant, this may be addressed *via* the use of two-colour excitation schemes in which the metastable state is in resonance with one of the laser frequencies. To provide maximum flexibility and elemental coverage, a two-colour CW laser system was employed. A twin laser system allows a variety of excitation schemes to be used, combining single color, two color, multiphoton excitation and combinations thereof.

A multi-slit assembly was included in the instrumentation for simultaneous detection of major isotopes, to be monitored via conventional detectors, to allow isotope ratio measurements. This will also provide reference beams so that the performance of the sample introduction system and ICP ion source can be monitored continuously and optimized.

The invention will now be illustrated, but in no way limited, with reference to the following examples and the accompanying drawings, in which,

figure 1 is a schematic representation of a Coincidence Laser Spectrometer, and

figure 2 is a schematic representation of a multi-detector head including a detector based upon a Coincidence Laser Spectrometer.

Referring to figure 1, a coincidence laser spectrometer (1) comprises an optical detector (2) coupled to a voltage programmer flight tube (3), which tube is provided with a laser system (4) and a non-specific ion detector (D1). Charged beam steering optics (5) are situated adjacent to an exit port from the flight tube. The apparatus may be provided with beam dumping means (6) adjacent to spectrometer exit slits (7).

Referring to figure 2, a spectrometer assembly (8) comprises a multi-slit assembly (9) coupled to conventional ion-detectors (10 and 11) and a coincidence laser spectrometer (12) (as defined by figure 1).

Example 1

Verification of Instrument Performance – Determination of Low Abundance Isotopes, e.g. ^{10}Be

The operating characteristics of the system were established *via* an established CLS transition, *e.g.*, the Be (II) line at 313 nm which is readily accessible to a CW tunable laser. Beryllium is an important element in its own right and its high mass isotope (^{10}Be) is an important geochronometer. It is produced by nuclear spallation of oxygen by cosmic rays and reaches an equilibrium concentration in surface quartz of about 2 x 10^7 atoms per g^{-1}. An isobaric interference with ^{10}B exists, but this can be resolved in the optical detector. A reasonable measurement of ^{10}Be was made by processing of a 5g solution after removal of the major matrix elements. Other cosmogenic isotopes that might be amenable to detection include those of K, Cs, Ca, Mn, Ni, Pd, Al and the lanthanides depending on identifying suitable spectroscopic transitions.

Example 2

Determination of Pu in Urine for Bioassay Purposes.

An aliquot of urine was spiked with a Pu tracer, processed to remove the bulk of the matrix and yielded a final sample volume of 1 cm^3. This sample was analyzed by ICP-MS-CLS using a low flow sample introduction system. The isotope ratios of ^{238}Pu, ^{239}Pu, ^{240}Pu with respect to the tracer isotope were estimated. The tracer isotope was monitored on a conventional detector whilst the isotopes of interest were determined using CLS detection. Isobaric interferences from, for example, $^{238}U^+$, $^{238}U^1H^+$, $^{204}Pb^{35}Cl^+$, ^{241}Am, were resolved optically in the CLS detector. A complete chemical separation of Pu from the matrix was not required and a simple, rapid, group separation of the actinides yielded a sample suitable for analysis by ICP-MS-CLS.

Example 3

Determination of Fundamental Nuclear Parameters

Optical isotope shifts and fine structure can be used to probe nuclei for the purpose of deriving fundamental nuclear data. The ICP-MS-CLS instrumentation allows the precise measurement of optical isotope shifts using the voltage programming facilities to bring isotopes into resonance selectively with the tuneable laser operating in frequency locked mode.

CLAIMS

1. An instrument comprising an Inductively Coupled Plasma Source Mass Spectrometer equipped with a multi-dimensional detector system wherein ions transmitted by the mass spectrometer are detected with high selectivity.

2. An instrument according to claim 1 wherein the multi-dimensional detector system comprises a plurality of sub-systems which provide a unitary response.

3. An instrument according to claim 2 wherein the multi-dimensional detector system comprises two sub-systems.

4. An instrument according to claim 3 wherein the sub-systems comprise a specific detector and a non-specific detector.

5. An instrument according to claim 3 wherein the two sub-systems of the multi-dimensional detector system are correlated temporally with high resolution.

6. An instrument according to claim 5 that provides co-incidence detection of transmitted ions.

7. An instrument according to claim 4 wherein the specific detector is based on optical spectrometry.

8. An instrument according to claim 7 wherein the specific detection of the transmitted ions is *via* resonance scattering processes.

9. An instrument according to claim 8 wherein the specific detection of the transmitted ions is *via* laser induced fluorescence.

10. An instrument according to claim 8 provided with means for collecting and detecting resonantly scattered photons efficiently.

11. An instrument according to claim 8 provided with means for the detection of the resonantly scattered photons with high temporal and spatial resolution.

12. An instrument according to claim 11 wherein the detection of resonantly scattered photons is *via* an imaging photomultiplier tube.

13. An instrument according to claim 4 wherein the second detector is a non-specific ion counting device.

14. An instrument according to claim 13 wherein the non-specific ion counting device is an electron multiplier.

15. An instrument according to claim 1 provided with means for manipulating the mean ion energy thereby reducing the relative spread of the ion beams energies.

16. An instrument according to claim 15 wherein the relative spread of ion beam energies may be manipulated to compress the optical bandwidth of the transmitted ions.

17. An instrument according to claim 15 provided with means for accelerating or decelerating the transmitted ion beam to manipulate the average ion beam energy and consequently the relative spread of ion beam energies.

18. An instrument according to claim 1 wherein a front-end collision/reaction cell is used to reduce the spread of the ion beam energies and compress the optical bandwidth of the transmitted ions.

19. An instrument according to claim 1 provided with means for manipulating the ion beam energies to bring the transmitted ion beam into resonance within the detection volume of the optical detector.

20. An instrument according to claim 19 provided with means for accelerating or decelerating the ion beam.

21. An instrument according to claim 7 wherein the ion beam is accelerated to induce an optical isotope shift by Doppler shifting.

22. An instrument according to claim 1 wherein a multiple exit slit assembly is incorporated.

23. An instrument according to claim 22 wherein the dual detector assembly is mounted upon the multiple slit assembly

24. An instrument according to claim 23 wherein the dual detector assembly is mounted upon the axial exit slit.

25. An instrument according to claim 22 wherein additional non-specific ion detectors are mounted upon the multiple exit slit assembly.

26. An instrument according to claim 25 wherein additional non-specific ion detectors are mounted upon the off-axis exit slits.

27. An instrument according to claim 26 wherein the non-specific ion detectors are electron multiplier devices.

28. A method for detecting and quantifying low concentrations of stable and/or radioisotopes and/or low abundance isotopes which comprises analysing a sample in an instrument according to claim 1.

29. A method according to claim 28 wherein the species being detected is a radionuclide.

30. A method according to claim 28 wherein selectivity is enhanced by specific optical detection of transmitted ions.

31. A method according to claim 28 wherein selectivity is enhanced by specific isotopic selection via optical isotope shifts.

32. A method according to claim 28 wherein selectivity is enhanced by inducing an optical isotope shift by acceleration of the transmitted ions with subsequent Doppler shifting.

33. A method according to claim 28 wherein selectivity is enhanced by optical probing of hyperfine splitting.

34. A method according to claim 28 wherein non-specific background is reduced by co-incidence detection of transmitted ions with subsequent improved detection limit.

35. An instrument substantially as described with reference the accompanying examples and drawings.

1/2

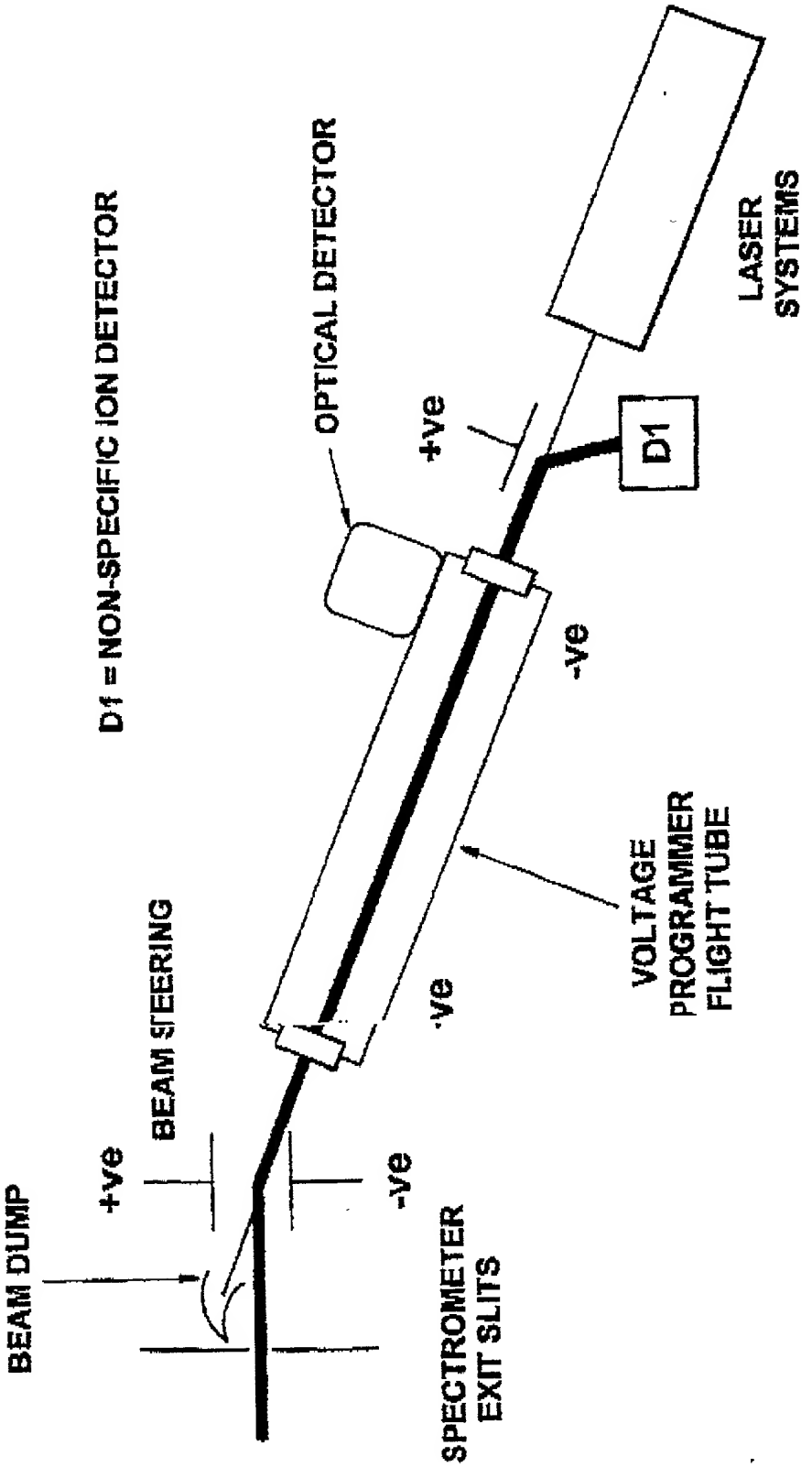
D1 = NON-SPECIFIC ION DETECTOR
OPTICAL DETECTOR
LASER SYSTEMS
+ve
D1
-ve
VOLTAGE PROGRAMMER
FLIGHT TUBE
-ve
BEAM STEERING
+ve
-ve
BEAM DUMP
SPECTROMETER EXIT SLITS

Fig. 1

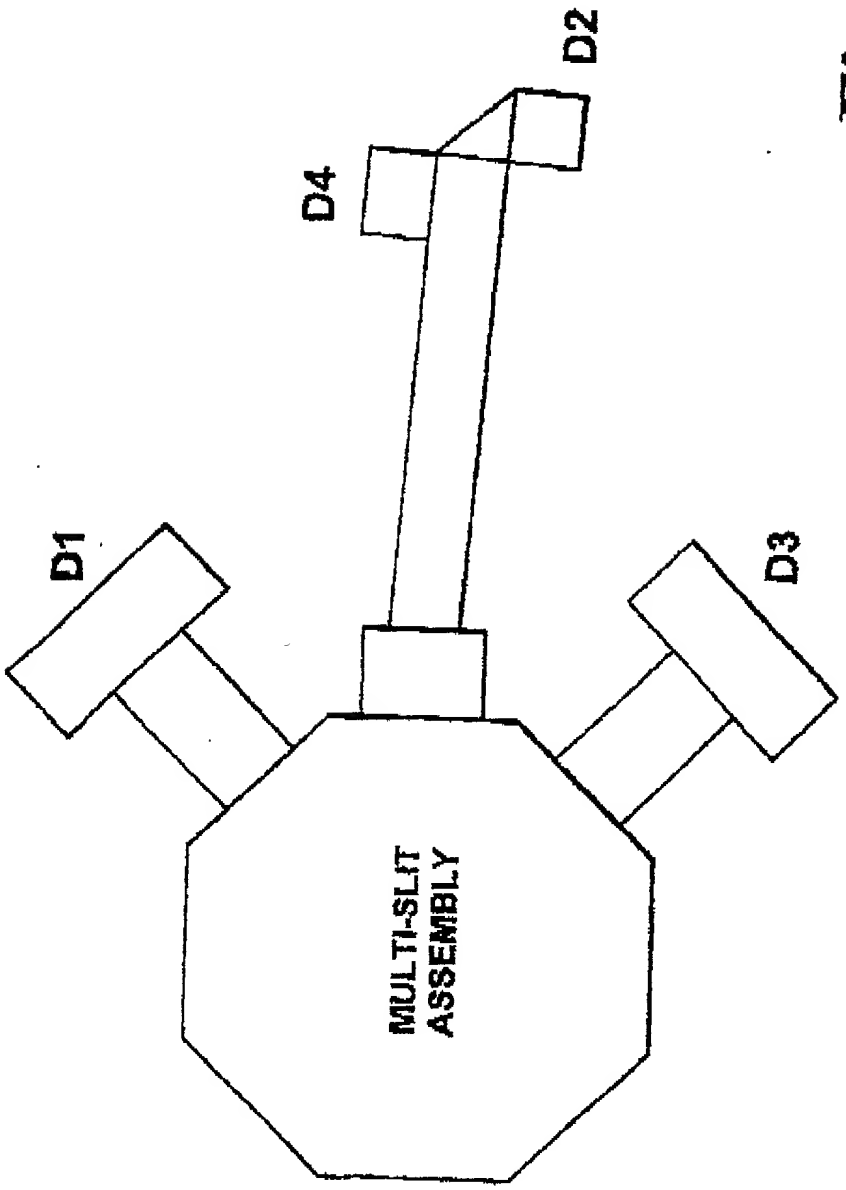

Fig. 2

D1-3 = CONVENTIONAL ION DETECTION
D4 = OPTICAL DETECTOR
N.B. A THREE SLIT ASSEMBLY HAS BEEN SHOWN FOR EXAMPLE ONLY

#5

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

Attorney Docket No. 9052-89

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **ANALYTICAL INSTRUMENT**,

the specification of which

☐ is attached hereto

OR

☒ was filed on **February 18, 2000** as PCT International Application No. **PCT/GB00/00577**.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or of any PCT International application having a filing date before that of the application on which priority is claimed.

9904289.7	GB	February 25, 1999	☒ Yes ☐ No
Number	Country	MM/DD/YYYY Filed	Priority Claimed
			☐ Yes ☐ No
Number	Country	MM/DD/YYYY Filed	Priority Claimed
			☐ Yes ☐ No
Number	Country	MM/DD/YYYY Filed	Priority Claimed

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below.

None	
Application Number(s)	Filing Date (MM/DD/YYYY)
Application Number(s)	Filing Date (MM/DD/YYYY)

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) or § 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application(s) in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application (37 C.F.R. § 1.63(d)).

PCT/GB00/00577	18 February 2000	Published
Appln. Serial No.	Filing Date	Status Patented/Pending/Abandoned
Appln. Serial No.	Filing Date	Status Patented/Pending/Abandoned
Appln. Serial No.	Filing Date	Status Patented/Pending/Abandoned

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following registered attorney(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. I also appoint the following registered attorney(s) to represent me before all competent International Authorities in connection with any and all international applications filed by me with an appropriate receiving office claiming priority to the U.S. application. I also appoint the following registered attorney(s) to make or receive payment on my behalf in connection with the filing of such international applications.

Customer Number 20792

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